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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07K 1/107, A61K 38/00	A3	(11) International Publication Number: WO 96/39422 (43) International Publication Date: 12 December 1996 (12.12.96)
(21) International Application Number: PCT/US96/09377 (22) International Filing Date: 6 June 1996 (06.06.96) (30) Priority Data: 08/466,610 6 June 1995 (06.06.95) US (71) Applicant: ALZA CORPORATION [US/US]; 950 Page Mill Road, P.O. Box 10950, Palo Alto, CA 94303-0802 (US). (72) Inventor: HOLLADAY, Leslie, A.; 1200 Dale Avenue #96, Mountain View, CA 94040 (US). (74) Agents: MILLER, D., Byron et al.; Alza Corporation, 950 Page Mill Road, P.O. Box 10950, Palo Alto, CA 94303-0802 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 6 March 1997 (06.03.97)
(54) Title: MODIFICATION OF POLYPEPTIDE DRUGS TO INCREASE ELECTROTRANSPORT FLUX (57) Abstract Methods of modifying polypeptide drugs in order to enhance their transdermal electrotransport flux are provided. The polypeptide is modified by substituting a histidine residue (His) for one or more glutamine (Gln), threonine (Thr) and/or asparagine (Asn) residue(s). The His for Gln substitution is particularly preferred from the standpoint of retaining biological activity of the parent polypeptide. Compositions containing the modified polypeptide, which are useful for transdermal electrotransport delivery, are also provided.		

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GA	Gabon			VN	Viet Nam

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/09377

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 C07K1/107 A61K38/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 628 043 A (SPIESS JOACHIM ET AL) 9 December 1986 see column 14, line 46 - column 16, line 15; claims; example X ---	1-5,7,8, 10,11, 13,15-19
P,A	EP 0 667 355 A (HOECHST AG) 16 August 1995 see claims; examples ---	1,5-7, 12-15
A	EP 0 643 981 A (TAKEDA CHEMICAL INDUSTRIES LTD) 22 March 1995 see claims; examples ---	1,5-7, 12-15
A	WO 95 11988 A (AFFYMAX TECH NV ;OLDENBURG KEVIN R (US); SELICK HAROLD E (US)) 4 May 1995 see claims; examples ---	1-19
	--- -/-	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

24 January 1997

Date of mailing of the international search report

04.02.97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax (+31-70) 340-3016

Authorized officer

Fuhr, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/09377

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 93 25197 A (AFFYMAX TECH NV ;HALE RON L (US); LU AMY (US); SOLAS DENNIS (US);) 23 December 1993 see claims; examples -----</p>	1-19

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/09377

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-14
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

* see continuation-sheet PCT/ISA/210 *
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 96/ 09377

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

Claims searched incompletely: 1-14

In view of the extremely large number of compounds falling under the claims 1-14, and of the absence of any technical support for these compounds in the description, the International Searching Authority considers that it is not economically reasonable to draw a search report covering the entire subject matter characterized above.

The search has therefore been limited to the real examples given in the description and closely related ones and includes compounds having the alleged activities.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/09377

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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